Program/Abstract # 443
Novel signals guiding endodermal progenitor cells toward pancreatic fate
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Commitment of multipotent endodermal cells to pancreatic fate occurs as a multistep process that eventually leads to a mature pancreas. While much is known about how the pancreas undergoes differentiation, growth and morphogenesis, we know little about early pancreatic specification. In particular, important gaps still persist in our knowledge of molecular players acting between endoderm specification and initiation of pancreatic organogenesis. In previous studies in *Xenopus* we identified the signaling factor Shirin as a novel player in early pancreas development. The *Xenopus* gene shows high similarity to a unique human RhoGAP gene, named *DLC2*. Very little is known about the function of this gene and, in particular, no embryological function has been assigned to it in mammals. Here, we show that Shirin is specifically expressed in the endoderm and pancreatic buds from gastrulation onwards both in frog and mouse embryos, representing one the earliest markers of pancreatic endoderm. Gain-of-function experiments in *Xenopus* indicated that Shirin alone is sufficient to induce pancreatic identity in the embryo, acting as an instructive factor. In line with this, we observe defects in pancreas formation upon conditional ablation of the *Shirin* gene expression in the mouse pancreatic endoderm. In particular, Shirin conditional knockout mouse exhibits severe pancreatic hypoplasia, possibly due to a reduction in the number of specified pancreatic progenitors. All together, gene expression profile and functional studies suggest a conserved role for Shirin at very early stages of the cascade of events leading to the specification of vertebrate pancreatic fate.

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Program/Abstract # 444
Notch signaling is important for epithelial and mesenchymal organization in the prostate gland
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Signaling by the Notch receptors has been implicated in the maintenance and differentiation of the pluripotent progenitors in the mammalian pancreas, intestine and vasculature. We have shown previously that during prostate development, Notch signaling is localized to the forming prostate buds and distal tips (Grishina et al., 2005). Here, we employed the $Nkx3.1^{Cre}$; $Rosa^{Notch1IC}$ and $Nkx3.1^{Cre}$; $RBP\text{-}J^{loxP}$ bi-genic mouse systems to analyze the effect of gain and loss of Notch function during embryonic and postnatal prostate development. We found that constitutive Notch signaling in the embryonic prostate resulted in a two-fold increase in p63-positive epithelial progenitors. In contrast, loss of the Notch mediator, *RBP-J* , resulted in significant changes in differentiation of both the epithelial and mesenchymal compartments. Analysis of *RBP-J* null postnatal prostates showed a two-fold decrease in cell proliferation in the epithelial ducts and the periductal mesenchyme. Mutant prostate epithelium failed to differentiate into luminal and basal compartments. Instead, *RBP-J* null prostate ducts consisted of a single layer of a simple cuboidal epithelium co-expressing both the basal and luminal markers. *RBP-J* null prostates also showed abnormally thin smooth muscle envelops indicating that Notch-dependent paracrine signaling is important for condensation and proliferation of the myocytes. Thus, our studies indicate that Notch pathway is important for progenitor proliferation, differentiation and organization both of the epithelium and mesenchyme of the prostate gland.

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Program/Abstract # 445
The role of Notch signaling in the bile duct development
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The mammalian biliary system is a highly branched network, consisting of intrahepatic and extrahepatic bile ducts. Dysfunction of bile ducts causes the accumulation of bile in the liver leading to liver damage, which is a major cause of liver disease. Recent studies have suggested that Notch signaling is necessary for normal bile duct formation, but its mechanism remain unclear. Here we used genetically altered mice to achieve liver-specific activation or blocking of Notch signaling. Our studies show that activating Notch signaling in liver progenitor cells is sufficient to promote the biliary cell differentiation, while blocking Notch signaling results in a reduced number of biliary cells and bile ducts. Notch signals are also required for biliary morphogenesis, and activation of Notch signaling in the hepatic lobule promotes ectopic biliary differentiation and tubulogenesis in a dose-dependent manner. Remarkably, activation of Notch signaling in adult hepatocytes is able to reprogram the hepatocytes into a biliary fate, the process of which recapitulates features of normal biliary development. Our ChIP study suggests that Notch signaling directly regulates the expression of a transcription factor Sox9 which is a potential candidate to mediate the effect of Notch in biliary development. Our results suggest that Notch signaling plays an essential role during liver development by coordinating biliary differentiation and morphogenesis.

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Program/Abstract # 446
Nuclear receptor NHR-25 interacts with Wnt/β-catenin signaling to direct differentiation of the *C. elegans* T cell
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Asymmetric cell divisions give rise to cells with distinct developmental fates, thus allowing formation of various cell types during organ differentiation. The worm *Caenorhabditis elegans* is extensively used to study cell fate determination, since its development relies heavily on asymmetric cell divisions. The epidermal stem cells, called seam cells, divide asymmetrically to produce a copy of themselves and a differentiated cell during postembryonic development. Here, we focus on the seam cell T, whose asymmetric division depends on a Wnt/β-catenin signaling pathway. We show that an impaired function of the nuclear receptor NHR-25 abolishes differentiation of the neural T cell lineage similarly to mutations in Wnt/β-catenin asymmetry signaling pathway components. By means of genetic interaction we demonstrate that NHR-25 cooperates with the Wnt/β-catenin pathway and with a parallel RUNX signaling to establish the correct fate of T cell daughters. Strikingly, the positive interaction between NHR-25 and Wnt/ catenin signaling in the T cell has an opposite character than in the *C. elegans* somatic gonad, where NHR-25 was shown to antagonize a β-catenin pathway (Asahina et al. 2006; Dev Cell 11, 203-). Therefore, the nuclear